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GC or not GC, that is the question:

The possibility of false positive results for gonorrhea in women at low risk for sexually transmitted disease

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The following article is a reprint of an article that appeared in the Epi-Sode Newsletter published by the Clark County Health Department in Vancouver, Washington. It is being republished with their permission.

Case 1: A white female in her 30s was seen for a physical examination and woman's health check. She had a slight vaginal discharge and no other symptoms. She was married and had been in a long-term monogamous relationship. A combined chlamydia/gonorrhea nucleic acid amplification test (NAAT) was obtained and results were positive for *Neisseria gonorrhoeae*. The patient questioned the accuracy of the test result and later went to another clinic for repeat testing. The results of the second test were negative for gonorrhea. Her husband was seen by his physician and tested two times. Both results were negative for chlamydia and gonorrhea.

Background: During the period January through March 2004, Clark County health care providers and laboratories reported thirty-seven female cases of *N. gonorrhoeae* to the health department. The department's Disease Investigation Specialist (DIS) conducted standard

interviews and identified several women for whom the positive results for gonorrhea were unexpected because they occurred in women who were either married or in long-term monogamous relationships. Subsequent testing in the women or their partners was negative for *N. gonorrhoeae*. A systematic review noted 11 (30%) of the total 37 cases suggested false positive results. The women were understandably highly concerned about the situation. The DIS brought this issue to the attention of the Health Officer, prompting a larger investigation to determine the reasons for discordant laboratory results. For the purpose of this article, we have included information from five case-patients. What follows is a summary of the investigation.

continued on page 2

Practice Guidelines

The following practice guidelines have been developed by the Clinical Laboratory Advisory Council. They can be accessed at the following website:

www.doh.wa.gov/lqa.htm

Anemia	Lipid Screening
ANA	Point-of-Care Testing
Bioterrorism Event Mgmt	PSA
Bleeding Disorders	Rash Illness
Chlamydia	Red Cell Transfusion
Diabetes	Renal Disease
Group A Strep Pharyngitis	STD
Hepatitis	Thyroid
HIV	Tuberculosis
Infectious Diarrhea	Urinalysis
Intestinal Parasites	Wellness

Inside This Issue

- 2-4 GC or not GC, cont'd
- 5 PHL Training Classes
- 6 Approved PT Providers/Calendar of Events

GC or not GC,

continued from page 1

Case definition: A false-positive case-patient was defined as a female patient reported to the health department, from January through March 2004, with gonorrhea based on a positive test by chlamydia/gonorrhea NAAT who did not have clinical symptoms suggestive of gonorrhea and who:

1. subsequently tested negative for *N. gonorrhoeae* without a course of antibiotics and/or
2. whose sexual partner tested negative for *N. gonorrhoeae*.

Investigation: Informed consent was obtained from the five case-patients. All five women had been screened for STDs using NAAT. The gonorrhea case report form was reviewed and abstracted. Incidence rates of gonorrhea in women in Clark County were calculated for the period 1999 through 2003 based on reported cases. Since January 2003, Clark County has been collaborating with CDC, Washington State Department of Health, and other local public health agencies in a supplemental gonorrhea behavioral surveillance project (Outcomes Assessment through Systems of Integrated Surveillance, OASIS). OASIS interviews from 25 women with positive results for gonorrhea reported January through March 2004 were reviewed for information about sexual history.

Findings: Of the five case-patients, only one was noted to have a vaginal discharge as the reason for medical visit. All five women were considered low risk based on sexual history (i.e. marriage or only one sexual partner in the past 90 days) and three of the women were 30 years or older. In addition, two of the women without a course of medication had subsequent negative tests, and all five women identified one male partner, each of whom subsequently tested negative for *N. gonorrhoeae* (see table on page 3). In 2003, 111 female cases of gonorrhea were reported to the department. This represented a 48% increase from 75 cases reported in 2002. Although this continued an upward trend in the incidence of gonorrhea in women which had first been noted in 2001, the increase in 2003 was more marked (see figure on page 3). Of interest, over 90% of the women interviewed in the OASIS study reported only one sexual partner in the previous three months and 36% were 30 years of age or older.

Sensitivity, specificity and the importance of prevalence for deciding GC or not GC.

Sensitivity = the proportion of real (true) infections identified by a screening test, 80% to 90% for NAAT. Specificity = the proportion of truly non-diseased people ruled out by the screening test, 97% to 99% for NAAT. Positive Predictive Value = the probability that a person testing positive for a disease actually has this disease, which depends on the specificity and the prevalence of the disease in a given community. In Clark County, the prevalence of gonorrhea in women is estimated to be <1%, meaning if 100 women at low risk for gonorrhea are screened with NAAT, only about 50% of those that test positive will actually have gonorrhea.

NAAT: There are currently three NAATs on the market and available in laboratories. Each of the three uses a different collection system. Therefore, a specimen collected for one NAAT cannot be run on another NAAT. The basic principle behind all of these tests is to identify the presence of small specific GC DNA strands by making thousands to millions of copies. If GC is present, then finding it changes from looking for a needle in a haystack (of DNA) to having an entire giant haystack of just GC DNA which is easy to find and identify. These tests do not require the preservation of live organisms. This results in several advantages for the test. The specimen requirements are less stringent as we do not need to keep GC bacteria alive. The tremendous magnification of the bacteria of interest (GC) makes it easy to find. Both of these features make NAATs much more sensitive for detecting the presence of GC bacteria in

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continued on page 3

GC or not GC,

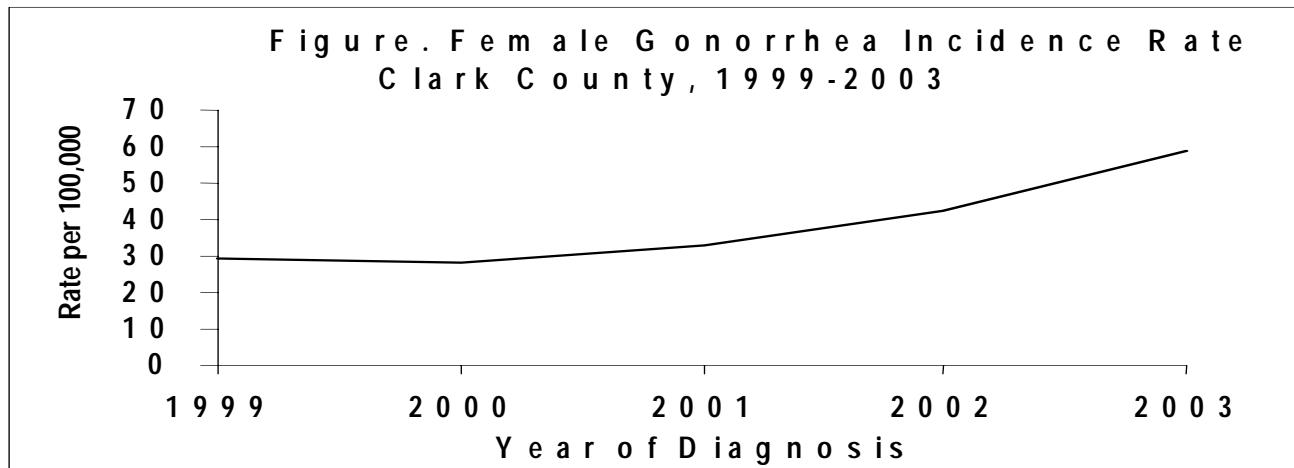
continued from page 2

Table. Selected reports of unanticipated positive results for gonorrhea in female case-patients, Clark County, January through March 2004

Case	Age group	Reason for visit	Results of NAAT*	Partner result	Marital status
			First test	Repeat test	Sexual history
1	30-34	Routine	Positive	Negative	Married
2	20-24	Exposed to CT**	Positive	Negative	One partner
3	15-19	Routine	Positive	-	Married
4	30-34	Vaginal discharge	Positive	-	Married
5	40-44	Routine	Positive	-	One partner

*Nucleic Acid Amplification Test

***Chlamydia trachomatis* infection



clinical specimens. The introduction of NAAT in the last few years is a step forward in laboratory science and an important technology for early detection of STDs. NAAT was introduced by Vancouver area laboratories in 2002 to 2003.

Discussion:

The five women in this case series were screened positive for gonorrhea using NAAT, but they were unlikely to have true gonococcal infection based on lack of symptoms, low risk sexual history, follow-up testing, and partner evaluation. In addition, enhanced interviews of women reported with gonococcal infection in 2004 did not find evidence of high risk sexual behavior*.

The evidence from this investigation suggests a positive test for gonorrhea in a woman without a risk history or symptoms may be a false positive and begs for further patient-provider dialogue. Similar findings of false positivity for gonorrhea using a specific NAAT have recently been reported¹. From the perspective of women marked as having gonorrhea, who really do NOT have gonorrhea, this information may have huge social and psychological impact. Dear Abby summed it up: *these inaccurate tests have victimized many people by creating havoc in their marriages.*² It is commendable that the DIS listened to these women and questioned the validity of the test results.

GC or not GC, continued from page 3

Recommendations:

For clinicians: When considering STD screening in sexually active women, it is advisable to take a sexual history to identify women at high risk. At a minimum, we suggest asking these three questions:

1. *Are you sexually active with men, women, or both?*
2. *How many partners have you had in the last year?*
3. *Does your male sexual partner have sex with men?*

Also, it is important to interpret test results in the context of age, sexual history, and physical examination. In Washington State and Clark County, the highest incidence of gonorrhea is reported in 15 to 24 year olds, so a clinician might question a positive result for gonorrhea in an older woman. To be on the safe side, for patients with a positive test for gonorrhea, it is a good idea to offer treatment right away, but also tell them it would be okay to wait to treat while another test was pending, as long as they were asymptomatic and did not expose anyone new. If the patient is younger than 25 years old, you might want to encourage treatment. The health department is available for consultation whenever there are questions.

For laboratorians: When STD screening is conducted in a population with low prevalence, CDC advises *consideration should be given to routinely performing an additional test after a positive screening test, if the positive predictive value is considered low (e.g. < 90%).*³

*A common sense definition of women at high risk of acquiring gonorrhea includes those who have multiple sequential or concurrent sex partners; women who have sex with men who have sex with men; and women with a history of gonococcal infection in the past 12 months.

The authors wish to acknowledge the contribution of Dr. Mary Ann Ware, STD/TB Medical Director, Multnomah County Health Department, Portland, Oregon, in reviewing the content of this article.

¹ Katz AR, Effler PV, Ohye RG, Brouillet B, Lee MVC, Whiticar PM. False-positive gonorrhea test results with a nucleic acid amplification test: the impact of low prevalence on positive predictive value. Clin Infect Dis 2004; 38:814-19.

² Van Buren A. Errors in venereal-disease tests can put strain on marriage. The Seattle Times 1990 October 15; Sect. E:9.

³ Centers for Disease Control and Prevention. Screening tests to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections - 2002. MMWR Morb Mortal Wkly Rep 2002;51(RR-15):1-40.

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11th Annual Clinical Laboratory Conference

The 11th Annual Clinical Laboratory Conference will be held on November 8, 2004, at the Seattle Marriott Hotel near Sea-Tac International Airport. This is an excellent opportunity to hear about the current status of health care from a variety of experts.

The program committee is in the process of finalizing the program. Dennis Weissman, President and Publisher of Washington G-2 Reports in Washington, D.C., will present the keynote address for the Conference. Meera Kanhouwa, MD, MHA, FACEP, Medical Director, Information Services at Swedish Medical Center in Seattle, has agreed to present an update on the *Patient Safety Institute*. Mark Stern, MD, Medical Director of the Washington State Department of Corrections, will present information on *Evidence-based Medicine*. Paul Keoppel, Compliance and Billing Administrator at Intermountain Health Care in Salt Lake City, Utah, will present a session on *Reducing Write-offs due to CMS Medical Necessity Rules*. It promises to be an excellent program.

Program flyers and registration forms were mailed in September. If you did not receive your copy, contact Leonard Kargacin (206) 361-2804 or leonard.kargacin@doh.wa.gov.

Basic Parasitology Training Course Series Registration Form

Name: _____
 Employer: _____
 Employer Address: _____
 City: _____ State: _____ Zip: _____
 Work Phone: _____ FAX: _____
 E-mail: _____ Message Phone: _____

Class preference: (check as many as applicable) **Complete Parasitology Series, Parts I-IV**

Part I: Nematodes, Nov. 9 & 10, 2004 **Part II: Protozoans, Jan. 12 & 13, 2005**

Part III: Trichromes, March 23 & 24, 2005 **Part IV: Blood Parasites, June 8 & 9, 2005**

HOW TO REGISTER: Complete the registration form and mail to the Department of Health, PHL Training Program 1610 NE 150th Street * PO Box 550501*Shoreline, WA 98155-9701 or fAX to: (206) 361-2904. A confirmation packet will be sent to you by mail. The packet will contain your registration confirmation, payment instructions and a map to the course location. Please **do not** send money with your registration form. **Tuition: \$210 each class or \$799 for the complete series.** Registration Deadlines: 2 weeks prior to class dates. A late registration fee of \$10 will be added for registrations received after the deadline. Visit our website at www.doh.wa.gov/ehsphl/phl/train/htm for more information.

Shipping & Handling of Biohazardous Materials Training Class

DATE, TIME & LOCATION: January 20, 2005 from 8:15 a.m. to 12:30 p.m at the DOH Public Health Laboratories in Shoreline, WA.

COURSE OBJECTIVES: Due to the changes in the hazardous shipping regulations, this workshop is being offered in order to update laboratory professionals. If your lab transports specimens or cultures via the US Postal Service, private vehicle (public health nurse), or overnight air (FED EX, Airborne Express), then you will want to attend this course. According to the Department of Transportation, employers must certify the training of their employees who ship hazardous materials.

Shipping and Handling of Biohazardous Materials Training Course Registration Form

Name: _____
 Employer: _____
 Employer Address: _____
 City: _____ State: _____ Zip: _____
 Work Phone: _____ FAX: _____
 E-mail: _____ Message Phone: _____

HOW TO REGISTER: Complete the registration form and mail to the **Department of Health, Training Program, 1610 NE 150th Street, PO Box 550501, Shoreline, WA 98155-9701** or fax to **206-361-2904**. A confirmation packet will be sent to you by mail. The packet will contain your registration confirmation, payment instructions and a map to the course location. Please **do not** send money with your registration form. **Tuition: \$85 if registered on or before January 6, 2005, or \$95 thereafter.** Visit our website at www.doh.wa.gov/ehsphl/phl/train/htm for more information.

Approved PT Providers

Accutest (800) 356-6788

<http://www.digitalpt.com>

Amer. Acad. of Family Physicians (800) 274-7911

<http://www.aafp.org/pt.xml>

Amer. Assoc. of Bioanalysts (800) 234-5315

<http://www.aab.org/>

American Proficiency Institute (800) 333-0958

<http://www.api-pt.com/>

ASIM Medical Lab Evaluation (800) 338-2746

<http://www.acponline.org/mle/>

California Thoracic Society (714) 730-1944

<http://www.thoracic.org/chapters/california/>

College of American Pathologists/EXCEL (800) 323-4040

<http://www.cap.org/apps/cap.portal>

WSLH (800) 462-5261

<http://www.slh.wisc.edu/pt/>

For answers to your PT questions, go to the LQA website at www.doh.wa.gov/lqa.htm or call Leonard Kargacin at (206) 361-2804.

Calendar of Events

PHL Training Classes:

(<http://www.doh.wa.gov/EHSPHL/PHL/train.htm>)

Parasitology Part I: Helminths

November 9 & 10 Shoreline

Handling & Shipping of Biohazardous Materials

January 20, 2005 Shoreline

11th Annual Clinical Laboratory Conference

November 8 Seattle

2005 WSSCLS/NWSSAMT Spring Meeting

April 28-30, 2005 Spokane

Northwest Medical Laboratory Symposium

October 26-29, 2005 Seattle

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion.